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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/520,781	01/11/2005	Yoshihiro Urade	2005_0021A	2424

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EXAMINER	
JEAN-LOUIS, SAMIRA JM	

ART UNIT	PAPER NUMBER
1617	

MAIL DATE	DELIVERY MODE
01/12/2009	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Advisory Action Before the Filing of an Appeal Brief	**Application No.** 10/520,781	**Applicant(s)** URADE ET AL.	
	Examiner SAMIRA JEAN-LOUIS	**Art Unit** 1617	

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 16 December 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:
   a) ☒ The period for reply expires *5* months from the mailing date of the final rejection.
   b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.

   Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
   (a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
   (b) ☐ They raise the issue of new matter (see NOTE below);
   (c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
   (d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.

   NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).
4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☐ Applicant's reply has overcome the following rejection(s): _____.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
   The status of the claim(s) is (or will be) as follows:
   Claim(s) allowed: _____.
   Claim(s) objected to: *4-7*.
   Claim(s) rejected: *3-7 and 10*.
   Claim(s) withdrawn from consideration: _____.

AFFIDAVIT OR OTHER EVIDENCE

8. ☒ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because: See continuation Sheet..
12. ☐ Note the attached Information *Disclosure Statement*(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/SREENI PADMANABHAN/
Supervisory Patent Examiner, Art Unit 1617

Applicant's arguments and Declaration from Dr.Yoshihiro Urade is acknowledged. However, applicant's arguments that the specification provides enablement for the entire genus of prostaglandin D receptor antagonists are not persuasive. It is the Examiner's contention that while applicant has demonstrated suppression of leakage due to brain injury utilizing cetain DP-type and CRTH2 type receptor antagonists, applicant has not demonstrated treatment or inhibition of brain injury utilizing all antagonists for prostaglandin D receptor in a patient in need thereof. Moreover, because of the variability found in the structures of antagonists for prostaglandin D receptor, one of ordinary skill in the art would not predictably concur that all prostaglandin D receptor antagonists can treat brain injury. Given that the skilled artisan must be able to readily recognize what structural features confer the antagonist properties of the prostaglandin D receptors and create another antagonist with the same desired characteristic, such determination would not be able to be ascertained without empirical, undue and unpredictable trial and error experimentation. Consequently, it is the Examiner's contention that applicant is not enabled for all antagonists for prostaglandin D receptor.

Applicant's arguments with regard to the objection of claims 4-7 has been fully considered but is not found persuasive. Because claim 3 remains rejected, such objection is also maintained.

Applicant's arguments that Tsuri et al. refer to allergic edema induced by allergen as opposed to edema in the brain has been fully considered. Applicant further argues that one of ordinary skill would not combine Tsuri and Wong. Such arguments are not persuasive as the rejection was made over the combined references of Tsuri in view of Wong. Tsuri et al. teach (ZS)-7-[(1R,2R,3S,5S)-2-(5-hydroxybenzo[b]tiophen-3-ylcarbonylamino)-10-norpinan-3yl]hept-5-enoic acid via modification of compound 14 using R-group 19 and compound (ZS)-7-[(1R,2R,3S,5S)-2-(5-benzo[b]tiophen-3-ylcarbonylamino)-10-norpinan-3yl]hept-5-enoic acid via modification of compound 14 using R-group 18 as potent selective antagonists of prostaglandin D2 receptors. Tsuri et al. further teach that these compounds are effective in reducing intranasal pressure largely due to their inhibition of vascular permeability (i.e. edema), reduction of smooth muscle cell (found in vascular cells) contractility as well as reducing the number of immune cells (i.e. eosinophils) infiltrates. Consequently, these data suggest that the aforementioned PGD2 receptor antagonists are helpful in reducing inflammation, edema, and vascular permeability. In the specification, applicant defined treatment of brain injury encompasses brain edema, cerebral bleeding (as a result of vascular permeability), and cerebrovascular disorders (see Applicant's specification, pg. 3, lines 15-24).
Wong et al., on the other hand, teach the pathophysiology associated with primary brain injury. Following brain injury, a primary inflammatory response is triggered which increases vascular permeability (i.e. Cerebral bleeding) and vasodilation that leads to vasogenic edema, cerebral ischemia and impaired autoregulation which consequently results in cytotoxic edema that exacerbates the existing cerebral ischemia resulting in secondary brain injury. Thus, in view of applicant's definition of the treatment of brain injury, one of ordinary skill in the art would have found it obvious to try and utilize the compounds of Tsuri et al. given their efficacy in inhibiting increases in microvascular permeability and their efficacy in reducing inflammation due to their effects on eosinophils. Moreover, one of ordinary skill in the art would have found it obvious to utilize the aforementioned compounds in the treatment of brain injury as brain injury is characterized by inflammation, edema formation and vascular permeability. In fact, applicant's arguments that DP receptor antagonists that are effective for brain injury are hard to determine is contradictory to applicant's recitation in claims 3 and 10 since these claims essentially recite the use of all DP receptor antagonists in treating brain injury. In fact, determining that all DP receptor antagonists would in fact entail undue experimentation. As a result, the Examiner asserts that the combined teachings of Tsuri in view of Wong do indeed render obvious applicant's invention.

Thus, the Examiner contends that the rejections of record were indeed proper and are therefore maintained.